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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,632	12/19/2001	Steve Sichuan Hc	38-21(51837)B	8916

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,632	HE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 7-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/19/01 &5/6/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/22/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-34 are pending.

2. Applicant's election with traverse of Group II, claims 3-6 including SEQ ID NO:2 filed 2/23/2004 is acknowledged. Applicant's arguments filed 2/23/2004 have been fully considered but they are not persuasive.

The traversal is on the ground(s) that it would not create an undue burden on the Examiner to conduct a search encompassing all of the claims (page 2 1st paragraph). The Office contends that while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office.

Applicants contend that the restriction to a single sequence is unduly burdensome on the applicant (page 2 1st paragraph). The Office contends that because of the vast number of sequences now present in the current databases that must be searched, the office does not have the resources to search more than one corresponding pair of nucleic acid and amino acid sequences per application.

Applicants contend that there is a single invention, inseparable into separate inventions, as each invention claimed by the office is closely related to and inseparable from every other invention described herein (page 2, 2nd paragraph). The Office contends that the restriction is justified based on arguments presented in the restriction requirement filed 12/19/2003.

Applicants point out that claims 3 and 4 of Group II and claim 7 of Group III are almost identical and there seems to be no basis for restriction between the two (page 3, 1st full paragraph). The Office contends that the claims in Group II are drawn to a specific nucleic acid encoding a specific protein identified by a sequence identifier, whereas the claims of Group III

are drawn to a recombinant DNA molecule encoding any ANT protein and method of using said recombinant DNA molecule. The method of Group III can use nucleic acid sequences other than those recited in the claims of Group II.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-2, and 7-34 are withdrawn from consideration because they are drawn to non-elected inventions.

3. Claims 3-6 are examined in the present office action.

Specification

4. The specification is objected to because Applicants have disclosed Figures 2A and 2B but the Brief Description of the Drawings only specifies Figure 2. Amending the Brief Description of the Drawings to include Figure 2A and 2B will obviate the objection.

Claim Objections

5. Claims 3-6 are objected to for reading on non-elected inventions. Correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide having an amino acid sequence that is substantially identical to SEQ ID NO:2, a nucleic acid molecule which hybridizes under stringent conditions to a nucleic acid molecule which encodes a protein with substantial identity to SEQ ID NO:2, or a nucleic acid sequence which encodes an amino acid sequence comprising SEQ ID NO:2 containing conservative amino acid substitutions.

Applicants isolated a cDNA clone from soybean, SEQ ID NO:1, that encodes SEQ ID NO:2, that shares sequence identity with the *Arabidopsis* ANT protein (pages 47-49, Example 1). Applicants disclose that SEQ ID NO:2 contains two AP2 DNA binding domains that share homology with the *Arabidopsis* ANT polypeptide, four conserved segments were identified in the N-terminal before the AP2 DNA binding domains, suggesting a possible functional role, and the C-terminal sequence of SEQ ID NO:2 bears little homology with that of the *Arabidopsis* ANT protein but does share conserved segments with another ANT-like clone isolated from soybean. Applicants suggest that these C-terminal segments may perform additional or distinguishable functions from the *Arabidopsis* ANT polypeptide (page 49, 2nd full paragraph).

The Applicants do not identify essential regions of SEQ ID NO:2 encoded by SEQ ID NO:1, nor do Applicants describe any polynucleotide sequences that hybridize to SEQ ID NO:1 and encode a functional protein comprising SEQ ID NO:2 or encode an amino acid sequence that

is substantially identical to SEQ ID NO:2. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding SEQ ID NO:2 falling within the scope of the claimed genus of polynucleotides, comprising sequences that encode polypeptides that are substantially identical to SEQ ID NO:2 or encode a protein with substantial identity to SEQ ID NO:2 or encode a polypeptide comprising SEQ ID NO:2 containing conservative amino acid substitutions. Applicants only describe a single cDNA of SEQ ID NO:1 encoding SEQ ID NO:2. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the protein of SEQ ID NO:2, it remains unclear what features identify the genus of nucleic acid sequences encoding the claimed genus of polypeptides exhibiting changes that

constitute substantially identical, substantial identity or polypeptides containing conserved amino acid substitutions. Since the genus of proteins of SEQ ID NO:2 have not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

7. Claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid sequences encoding SEQ ID NO:2 and plant transformation therewith, does not reasonably provide enablement for nucleic acid sequences encoding a polypeptide having an amino acid sequence that is substantially identical to SEQ ID NO:2, an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent conditions to a nucleic acid encoding SEQ ID NO:2 or an isolated nucleic acid sequence which encodes an amino acid sequence comprising SEQ ID NO:2 containing conservative amino acid substitutions and plant transformation therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide having an amino acid sequence that is substantially identical to SEQ ID NO:2, a nucleic acid molecule which hybridizes under stringent conditions to a nucleic acid molecule which encodes a protein with substantial identity to SEQ ID NO:2, or a nucleic acid sequence which encodes an amino acid sequence comprising SEQ ID NO:2 containing conservative amino acid substitutions.

Applicants isolated a cDNA clone from soybean, SEQ ID NO:1, that encodes SEQ ID NO:2, that shares sequence identity with the *Arabidopsis* ANT protein (pages 47-49, Example 1). Applicants disclose that SEQ ID NO:2 contains two AP2 DNA binding domains that share homology with the *Arabidopsis* ANT polypeptide, four conserved segments were identified in the N-terminal before the AP2 DNA binding domains, suggesting a possible functional role, and the C-terminal sequence of SEQ ID NO:2 bears little homology with that of the *Arabidopsis* ANT protein but does share conserved segments with another ANT-like clone isolated from soybean. Applicants suggest that these C-terminal segments may perform additional or distinguishable functions from the *Arabidopsis* ANT polypeptide (page 49, 2nd full paragraph). Applicants transformed *Arabidopsis* with SEQ ID NO:1 operably linked to the 35S promoter to produce plants with increased growth and biomass of the roots (page 72, 1st paragraph), increased floral size and increased seed size (page 73, Examples 28 and 29).

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that encode a polypeptide with substantial identity to SEQ ID NO:2 will encode a protein with

the same activity as a protein comprising the amino acid sequence of SEQ ID NO:2. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, would produce a polypeptide with substantial identity with SEQ ID NO:2. The nucleic acids encoding all these mutated

proteins, however, would hybridize under stringent conditions to the nucleic acids encoding the original protein.

Applicants' claims are drawn to nucleic acid sequences that hybridize to a nucleic acid sequence encoding a polypeptide with substantial identity to SEQ ID NO:2, but the state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by selecting random pieces of DNA as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed could produce plants with a morphology as specified by Applicant and

encode a protein with substantial identity with SEQ ID NO:2 or comprise a polypeptide with conservative amino acid substitutions.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Elliott et al (1996, The Plant Cell 8:155-168).

The claims are drawn to an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide having an amino acid sequence that is substantially identical to SEQ ID NO:2, a nucleic acid molecule which hybridizes under stringent conditions to a nucleic acid molecule which encodes a protein with substantial identity to SEQ ID NO:2, or a nucleic acid sequence which encodes an amino acid sequence comprising SEQ ID NO:2 containing conservative amino acid substitutions.

Ellott et al teach a nucleic acid sequence that encodes the Arabidopsis AINTEGUMENTA (ANT) protein that exhibits 38% sequence identity to Applicants' SEQ ID NO:2 (See enclosed sequence search results). Given that the encoded protein of Elliott et al is the *Arabidopsis* homologue to Applicants' polypeptide, the nucleic acid sequence of Elliott et al encodes a polypeptide that is substantially identical to SEQ ID NO:2, comprises conservative substitutions, and the isolated nucleic acid sequence of Elliott et al would hybridize under

stringent conditions to Applicants' sequence and encode a polypeptide with substantial identity to SEQ ID NO:2, and as such, Elliott et al anticipate the claimed invention. The Office interprets "stringent conditions" to mean moderately stringent conditions given that Applicant has not specifically stated the conditions and times at which the hybridization and wash were performed.

9. Claim 6 is deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated nucleic acid sequence encoding an amino acid sequence comprising SEQ ID NO:2.

10. Claim 6 is objected to but would be allowable if the claim was rewritten to over-come the objections as stated above.

11. Claims 3-5 are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
May 10, 2004